10/519,654

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1751	((514/252.14) or (514/275)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2006/11/14 10:36
L2	2642	((544/295) or (544/331)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2006/11/14 10:37
L3	3516	L1 or L2	US-PGPUB; USPAT	OR	OFF	2006/11/14 10:37
L4	2775	L3 and (pyridinyl or pyridyl or pyridine)	US-PGPUB; USPAT	OR	OFF	2006/11/14 10:38
L5	378	L4 and benzamide	US-PGPUB; USPAT	OR	OFF	2006/11/14 10:38
L6	227	L5 and (inflammatory or inflammation or antiinflammation or 'IL' or interleukin)	US-PGPUB; USPAT	OR	ON	2006/11/14 10:50
L7	1047	gleevec or imatinib	US-PGPUB; USPAT	OR	ON	2006/11/14 10:51
L8	834	L7 and (inflammation or inflammatory or antiinflammation or interleukin)	US-PGPUB; USPAT	OR	ON	2006/11/14 10:51
L9	51	L8 not cancer	US-PGPUB; USPAT	OR	ON	2006/11/14 10:52

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- Search numbers may not be continuous; all searches are represented.
- To save search indefinitely, click query # and select Save in My NCBI.
- To combine searches use #search, e.g., #2 AND #3 or click query # for more options.

Search	Most Recent Queries	Time	Result
#6	Search **gleevec and interleukin**	11:27:47	60
#5	Search **gleevec and inflammation**	11:26:14	21
#1	Search **fibroproliferation and inflammation**	11:21:52	37
#3	Search **fibroproliferation and inflammation and imatinib**	11:21:26	0
#2	Search **fibroproliferation and inflammation and gleevec**	11:21:07	0

Clear History

10/ 519,654

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NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 13	OCT 19	E-mail format enhanced
NEWS 14	OCT 23	Option to turn off MARPAT highlighting enhancements available
NEWS 15	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 17	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 18	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 19	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 20	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 21	NOV 13	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role

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10/ 519,654

FILE 'HOME' ENTERED AT 11:57:21 ON 14 NOV 2006

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	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'HCAPLUS' ENTERED AT 11:57:36 ON 14 NOV 2006
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FILE COVERS 1907 - 14 Nov 2006 VOL 145 ISS 21
FILE LAST UPDATED: 12 Nov 2006 (20061112/ED)

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=> s fibroproliferation and inflammat?
            80 FIBROPROLIFERATION
        255287 INFLAMMAT?
L1          39 FIBROPROLIFERATION AND INFLAMMAT?

=> s L1 not py>2001
       5548812 PY>2001
L2          18 L1 NOT PY>2001

=> d l2 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 18 ANSWERS - CONTINUE? Y/(N):y

L2   ANSWER 1 OF 18  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2001:659981  HCAPLUS
DOCUMENT NUMBER:         136:116864
TITLE:                   Fibroproliferative response in matrix deposition
AUTHOR(S):               Vignola, A. M.; Chiappara, G.; Siena, L.; Gagliardo,
                         R.; Chanez, P.; Bousquet, J.
CORPORATE SOURCE:        Institute of Respiratory Pathophysiology, CNR,
                         Palermo, 90146, Italy
SOURCE:                  Clinical & Experimental Allergy Reviews (2001), 1(2),
                         111-115
                         CODEN: CEARC3; ISSN: 1472-9725
PUBLISHER:               Blackwell Science Ltd.
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                English
AB   A review. Asthma may be characterized by an ongoing inflammatory
     process sustained by active inflammatory and fibroproliferative
     responses. Both of these responses may contribute to an imbalance of the
     mechanism regulating extracellular matrix synthesis and degradation leading to
     various structural alterations that can all contribute to an overall
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increase in airway wall thickness and have an important effect on lung function.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:586169 HCAPLUS
DOCUMENT NUMBER: 136:182041
TITLE: Type 1/type 2 cytokine paradigm and the progression of pulmonary fibrosis
AUTHOR(S): Lukacs, Nicholas W.; Hogaboam, Cory; Chensue, Stephen W.; Blease, Kate; Kunkel, Steven L.
CORPORATE SOURCE: Department of Pathology, University of Michigan Medical School, Ann Arbor, MI, 48109-0602, USA
SOURCE: Chest (2001), 120(1, Suppl.), 5S-8S
CODEN: CHETBF; ISSN: 0012-3692
PUBLISHER: American College of Chest Physicians
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The pathogenesis of end-stage, chronic lung disease is thought to be characterized by an initial inflammatory response followed by fibroproliferation and deposition of extracellular matrix. Many of these chronic lung disorders share a variety of common properties, including an unknown etiol., undefined mechanisms of initiation and maintenance, and progressive fibrosis. Unfortunately, efficacious therapeutic options are not readily available for the treatment of many chronic lung diseases, which may reflect the limited scientific and mechanistic understanding of these disorders. However, recent studies have shown that cytokine networks are likely operative in dictating the progression of these diseases, as these mediators can influence fibroblast activation, proliferation, and collagen deposition during the maintenance of chronic fibrotic lung disease. Accumulating data support the concept that the specific cytokine phenotype may provide a fundamental mechanism for the regulation or continuation of the fibrotic process. For example, interferon-γ appears to suppresses fibroblast activities, such as proliferation and collagen production, while interleukin (IL)-4 and IL-13 can augment fibroblast growth and collagen production Interestingly, these mediators are prototypic cytokines that functionally define either a type-1 or a type-2 immune response. Thus, exptl. models of cell-mediated lung inflammation, which are characterized by either a type-1 or a type-2 response, will be useful in delineating the mechanisms that either maintain or resolve chronic lung inflammation and accompanying fibrosis.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:274726 HCAPLUS
DOCUMENT NUMBER: 135:224980
TITLE: Matrix metalloproteinase (MMP)-2, MMP-7, and tissue inhibitor of metalloproteinase-1 are closely related to the fibroproliferative process in the liver during chronic hepatitis C
AUTHOR(S): Lichtinghagen, Ralf; Michels, Dirk; Haberkorn, Christian I.; Arndt, Burkhard; Bahr, Matthias; Flemming, Peer; Manns, Michael P.; Boeker, Klaus H. W.
CORPORATE SOURCE: Department of Clinical Chemistry, Medizinische Hochschule, Hannover, D-30623, Germany
SOURCE: Journal of Hepatology (2001), 34(2), 239-247
CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

10/ 519,654

AB Background/Aims: To study whether expression of matrix metalloproteinases and their inhibitors correlate with ongoing fibrogenesis, we measured hepatic mRNA levels of matrix metalloproteinase (MMP) -2, MMP-7, and MMP-9 as well as tissue inhibitor of metalloproteinase (TIMP) -1, TIMP-2, and TIMP-3 and compared it to histol., procollagen IV alpha-1 chain mRNA levels, and biochem. parameters in patients with chronic active hepatitis C (CAH). Methods: Quant. reverse transcription-polymerase chain reaction/enzyme-linked immunosorbent assay using in vitro transcribed competitor and standard RNA were performed from ten normal livers (N), 29 CAH liver biopsies and seven samples with hepatitis C virus (HCV)-induced end-stage cirrhosis (Ci). Results: From N to Ci both TIMP and MMP RNA expression increased. However, none of the RNA levels differed significantly between CAH patients with and without fibrosis. Non-parametric correlation anal. and receiver operating characteristics curves show that MMP-2, MMP-7, and TIMP-1 provide the best discrimination between cirrhosis and pre-cirrhotic stages. They also correlate with histol. and biochem. inflammatory activity and with procollagen IV mRNA. Conclusion: Hepatic fibroproliferation is associated with alterations of hepatic TIMP and MMP expression. The relation of hepatic TIMP and MMP mRNA levels to disease stage and inflammatory activity underlines their potential as diagnostic markers in chronic liver disease.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:587659 HCAPLUS

DOCUMENT NUMBER: 134:146239

TITLE: Elevated levels of interleukin-8 and transforming growth factor-beta in bronchoalveolar lavage fluid from patients with bronchiolitis obliterans syndrome: Proinflammatory role of bronchial epithelial cells

AUTHOR(S): Elssner, Andreas; Jaumann, Florian; Dobmann, Sandra; Behr, Jurgen; Schwaiblmair, Martin; Reichenspurner, Hermann; Furst, Heinrich; Briegel, Josef; Vogelmeier, Claus

CORPORATE SOURCE: "Munich Lung Transplant Group", Division for Pulmonary Diseases, Department of Internal Medicine I, Klinikum Grosshadern, Ludwig-Maximilians-University of Munich, Munich, 81366, Germany

SOURCE: Transplantation (2000), 70(2), 362-367
CODEN: TRPLAU; ISSN: 0041-1337

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background. Obliterative bronchiolitis (OB), the most important long-term complication after lung transplantation, is thought to be a manifestation of chronic rejection within the airways, with the hallmarks inflammation and fibroproliferation. Methods. To characterize the inflammatory process in the context of OB we quantified tumor necrosis factor-α, interleukin (IL)-8, IL-10, and transforming growth factor (TGF)-β on the protein and mRNA level in bronchoalveolar lavage fluid samples obtained from patients with bronchiolitis obliterans syndrome (BOS) and without BOS. In addition, bronchial cells sampled by bronchial brushing were analyzed for mRNA expression. Results. In respiratory epithelial lining fluid (ELF) from BOS patients the protein levels of IL-8 (52.4±22.2 vs. 4.4±0.9 pg/mL ELF, $P<0.005$) and TGF-β (5.6±1.9 vs. 0.9±0.2 ng/mL ELF, $P<0.005$) were significantly elevated. In addition, bronchoalveolar lavage fluid cells of BOS patients showed increased expression of TGF-β (1.13±0.44 vs. 0.45±0.16, optical d. [O.D.]/O.D. glyceraldehyde-3-phosphate dehydrogenase [GAPDH], $P=0.11$) and IL-8 (0.25±0.13 vs. 0.09±0.03 O.D./O.D. GAPDH, $P=0.53$) without the

differences reaching statistical significance. In contrast, IL-8 mRNA expression of bronchial cells was significantly higher in the BOS group (0.85±0.40 vs. 0.22±0.10 O.D./O.D. GAPDH, P<0.05). Conclusions. We assume that IL-8 and TGF-β may act as key mediators for airway inflammation and fibroproliferation in the pathogenesis of OB, with bronchial epithelial cells serving as a relevant source of IL-8.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:395257 HCAPLUS
DOCUMENT NUMBER: 133:118360
TITLE: Expression of matrix metalloproteinase-2 and -9 and their inhibitors in peripheral blood cells of patients with chronic hepatitis C
AUTHOR(S): Lichtinghagen, Ralf; Huegel, Omar; Seifert, Thomas; Haberkorn, Christian I.; Michels, Dirk; Flemming, Peer; Bahr, Matthias; Boeker, Klaus H. W.
CORPORATE SOURCE: Institute of Clinical Chemistry, Medizinische Hochschule, Hannover, D-30623, Germany
SOURCE: Clinical Chemistry (Washington, D. C.) (2000), 46(2), 183-192
CODEN: CLCHAU; ISSN: 0009-9147
PUBLISHER: American Association for Clinical Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: To clarify whether circulating matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) can be used as serum markers of fibroproliferation in chronic liver diseases, the authors studied the expression of MMP-2 and MMP-9 in relation to TIMP-1 and TIMP-2 in peripheral blood mononuclear leukocytes (MNLs) and polymorphonuclear leukocytes (PMLs), and compared this expression to circulating concns. and hepatic histol. in patients with chronic active hepatitis C (CAH). Methods: Quant. reverse transcription-PCR/ELISA assays were performed for MMP and TIMP RNA, and corresponding circulating protein concns. were studied by ELISA in 20 healthy controls, 40 patients with CAH, and 20 patients with hepatitis C-induced cirrhosis (Ci). Results: MMP-2 mRNA was found almost exclusively in the liver, MMP-9 mRNA in leukocytes. TIMP RNA-equivalent were decreased in MNLs of CAH patients, but neither MMP-9 nor TIMP RNA expression showed any correlation to the extent of inflammation and fibrosis. MMP-2 and TIMP-1 protein concns. were increased in Ci patients and showed a wide overlap in CAH patients and healthy controls. MMP-9 values were lower in CAH and Ci patients than in healthy controls. TIMP-2 values showed a wide overlap in all three groups. The MMP-2/TIMP-1 and MMP-9/TIMP-1 ratios were lower in Ci patients than in healthy controls; the MMP-2/TIMP-2 and MMP-9/TIMP-2 ratios were not different. Circulating TIMP-1 and the MMP-2/TIMP-1 ratio correlated to the inflammatory activity in liver biopsies, but only the circulating MMP-2/TIMP-1 ratio also correlated with the degree of fibrosis. Conclusions: Peripheral blood cell expression of MMP-2, MMP-9, and TIMP revealed no correlation with the circulating concns. of these proteins. Only the circulating MMP-2/TIMP-1 ratio correlated to the histol. degree of fibrosis in hepatitis C and should be further evaluated as a progression marker in patients with chronic liver disease.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:343945 HCAPLUS
DOCUMENT NUMBER: 133:250633
TITLE: Up-regulation of inducible nitric oxide synthase in fibroblasts parallels the onset and progression of

fibrosis in an experimental model of post-transplant obliterative airway disease
AUTHOR(S): Romanska, Hanna M.; Ikonen, Tuija S.; Bishop, Anne E.; Morris, Randall E.; Polak, Julia M.
CORPORATE SOURCE: Department of Histochemistry, Hammersmith Hospital, London, W12 ONN, UK
SOURCE: Journal of Pathology (2000), 191(1), 71-77
CODEN: JPTLAS; ISSN: 0022-3417
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The main cause of mortality following lung transplantation is chronic rejection, manifesting morphol. as obliterative bronchiolitis (OB). It has been suggested that damage to the respiratory epithelium initiates proliferation of mesenchymal cells, leading to dense collagenous scarring in small airways. Inducible nitric oxide synthase (iNOS) is strongly expressed in the damaged epithelium in human OB, along with high levels of peroxynitrite, suggesting that endogenous NO mediates the epithelial destruction. To examine further the role of iNOS in this process, heterotopic airway implants were studied in rats, an acknowledged disease model. Specimens of iso- or allografted trachea, collected 3-60 days after implantation, were processed for histol. and immunocytochem. for iNOS and, as a marker of peroxynitrite formation, nitrotyrosine. In both iso- and allografts at the earliest stage (day 3), ischemia was associated with severe epithelial damage or loss. These changes progressed until day 7 and were accompanied by strong expression of iNOS and nitrotyrosine in epithelial cells. In isografts, epithelial recovery was seen, with abundant iNOS immunoreactivity but little nitrotyrosine. In contrast, the epithelium in allografts did not regenerate and progressive inflammation and fibroproliferation occurred until complete obliteration of the tracheal lumen at day 60. The fibroproliferation was associated with changes in morphol. of fibroblasts that were accompanied by alterations in their iNOS expression. INOS immunoreactivity was dense in the plump fibroblasts of early lesions, in some cases as early as post-operative day 5, but very weak in elongated fibroblasts in totally occluded grafts. The intensity of immunoreactivity for nitrotyrosine corresponded to that of iNOS. These results indicate a dual role for NO in the airway obliteration that follows transplantation, through destruction of epithelium and stimulation of fibroblast activity.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:113042 HCAPLUS
DOCUMENT NUMBER: 132:161268
TITLE: Therapeutic uses for compounds which reduce c-jun gene expression
INVENTOR(S): Peterson, Theresa C.
PATENT ASSIGNEE(S): Dalhousie University, Can.
SOURCE: U.S., 20 pp., Cont.-in-part of U.S. Ser. No. 870,096.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6025151	A	20000215	US 1998-92317	19980605
US 5985592	A	19991116	US 1997-870096	19970605
CA 2262463	AA	19981210	CA 1998-2262463	19980605
US 6294350	B1	20010925	US 1999-433621	19991102
PRIORITY APPLN. INFO.:			US 1997-870096 A2	19970605

US 1998-92317 A2 19980605

AB In accordance with the invention, it has been discovered that monocyte conditioned medium (MCM) obtained from patients with liver disease stimulates the proliferation of fibroblasts. Platelet derived growth factor (PDGF) has also been found to stimulate fibroproliferation of fibroblasts, and to be at least partially responsible for the fibroproliferative effect of the MCM. Further, in accordance with the invention, the effect of MCM and PDGF on the expression of c-fos and c-jun has been investigated, because c-fos and c-jun form AP-1 complexes which can stimulate genes involved in proliferation. It has recently been reported that pentoxifylline inhibits platelet derived growth factor-stimulated proliferation. Studies were conducted to determine whether pentoxifylline altered the expression of c-fos and c-jun. While PDGF was found to induce the expression of both c-fos and c-jun, pentoxifylline was found to effectively reduce the effect of PDGF-induced c-jun gene expression, without altering c-fos gene expression. These results suggest that pentoxifylline inhibits PDGF-stimulated proliferation by decreasing c-jun expression. These results further suggest a variety of diseases and/or conditions which may also be successfully treated with compds., such as pentoxifylline, which reduce the transcription of c-jun gene.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:506863 HCAPLUS

DOCUMENT NUMBER: 131:321153

TITLE: Chemokines in lung injury. Thomas A. Neff lecture

AUTHOR(S): Strieter, Robert M.; Kunkel, Steven L.; Keane, Michael P.; Standiford, Theodore J.

CORPORATE SOURCE: Department of Internal Medicine, Division of Pulmonary and Critical Care Medicine, The University of Michigan Medical School, Ann Arbor, MI, USA

SOURCE: Chest (1999), 116(1, Suppl.), 103S-110S
CODEN: CHETBF; ISSN: 0012-3692

PUBLISHER: American College of Chest Physicians

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 80 refs. Acute lung injury is due to a variety of direct or indirect insults leading to pulmonary inflammation. Several clin. entities, including trauma, pneumonia/sepsis, and ischemia-reperfusion injury are characterized by varying degrees of pulmonary insult that result in functional impairment of gas transfer in the lung. These events lead to an inflammatory response that is characterized by the following: recognition of the site of injury by inflammatory cells; specific recruitment of subpopulations of leukocytes into tissue; removal of the offending agent and "debridement" of the injured cells/tissue; and repair of the site of injury with attempts to reestablish normal parenchymal, stromal, and extracellular matrix relationship. This is achieved by an orchestrated involvement of both innate and adaptive immunity. In contrast, normal resolution of acute lung injury may not be achieved. This may actually lead to the pathogenesis of pulmonary fibrosis with features of dysregulated repair with exaggerated neovascularization, fibroproliferation, and abnormal deposition of extracellular matrix, leading to progressive fibrosis and loss of lung function. For example, the host response to a bacterial pneumonia is characterized by an acute inflammatory reaction. The histopathol. of bacterial pneumonia is composed of proteinaceous exudate and massive neutrophil extravasation leading to consolidation of the lung. Once the inciting agent is cleared, the inflammatory reaction resolves and normal repair and tissue remodeling occurs. This reestablishes normal lung function without the sequela of chronic pulmonary fibrosis. In contrast, the acute inflammatory response associated with ARDS may culminate in severe

lung injury, impacting on resolution of inflammation. This injury may ultimately lead to pulmonary fibrosis, impaired gas transfer, and impact on patient survival. The basic mechanisms and mediators that induce acute pulmonary inflammation remain to be fully elucidated. However, it is known that the participation of a variety of factors, produced by both immune and nonimmune cells, is involved in the coordination of these activities, including reactive oxygen metabolites, carbohydrates, lipids, and protein mediators, such as cytokines.

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:301932 HCAPLUS
DOCUMENT NUMBER: 131:125233
TITLE: Effect of pentoxifylline on early proliferation and phenotypic modulation of fibrogenic cells in two rat models of liver fibrosis and on cultured hepatic stellate cells
AUTHOR(S): Desmouliere, Alexis; Xu, Guoxiong; Costa, Andrea M. A.; Yousef, Ibrahim M.; Gabbiani, Giulio; Tuchweber, Beatriz
CORPORATE SOURCE: GREF, Universite Victor Segalen Bordeaux 2, Bordeaux, 33076, Fr.
SOURCE: Journal of Hepatology (1999), 30(4), 621-631
CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During liver fibrosis, different fibroblastic cells, i.e. hepatic stellate cells (HSCs) or portal fibroblasts, are involved in the development of lesions, and acquire myofibroblastic differentiation. We investigated, in the rat, whether pentoxifylline can influence the early phase of fibrogenesis in two animal models of fibrosis induced by either carbon tetrachloride (CCl4) plus acetone (given twice) or bile duct ligation. The fibroproliferative response and myofibroblastic phenotypic modulation were evaluated by PCNA and alpha-smooth muscle (α-SM) actin immunohistochem., resp., in livers taken 24 h after the last CCl4 treatment or 72 h after bile duct ligation. Desmin expression was also measured, and inflammation was evaluated by ED-1 staining. Furthermore, proliferation and α-SM actin expression were studied in cultured HSCs after pentoxifylline treatment. In the CCl4-acetone groups, pretreatment with pentoxifylline decreased the proliferative response and expression of α-SM actin in the HSCs. Similarly, pentoxifylline reduced the proliferation and myofibroblastic differentiation of portal fibroblasts after bile duct ligation. Pentoxifylline reduced ED-1 expression, particularly in the CCl4 model, where there was significant inflammation. In cultured pentoxifylline-treated HSCs, both proliferation and α-SM actin expression were decreased. In both animal models of fibrosis, during the early stages of tissue injury, pentoxifylline was able to reduce fibroproliferation and myofibroblastic differentiation and to reduce hepatocellular damage and the inflammatory response, particularly in the toxin-induced model. In culture, α-SM actin expression decreased in both growing and quiescent HSCs treated with pentoxifylline, indicating that the drug may also exert a direct effect on hepatic fibrogenic cells.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:804173 HCAPLUS
DOCUMENT NUMBER: 130:49501
TITLE: New uses for compounds which reduce c-jun gene expression

10/ 519,654

INVENTOR(S): Peterson, Theresa C.
PATENT ASSIGNEE(S): Dalhousie University, Can.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9855110	A2	19981210	WO 1998-CA570	19980605
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5985592	A	19991116	US 1997-870096	19970605
CA 2262463	AA	19981210	CA 1998-2262463	19980605
AU 9880055	A1	19981221	AU 1998-80055	19980605
PRIORITY APPLN. INFO.:			US 1997-870096 A	19970605
			WO 1998-CA570 W	19980605

AB In accordance with the present invention, it has been discovered that monocyte-conditioned medium (MCM) obtained from patients with liver disease stimulates the proliferation of fibroblasts. Platelet-derived growth factor (PDGF) has also been found to stimulate fibroproliferation of fibroblasts, and to be at least partially responsible for the fibroproliferative effect of the MCM. Further in accordance with the present invention, the effect of MCM and PDGF on the expression of c-fos and c-jun has been investigated, because c-fos and c-jun form AP-1 complexes which can stimulate genes involved in proliferation. It has recently been reported that pentoxifylline inhibits platelet derived growth factor-stimulated proliferation. Studies were conducted to determine whether pentoxifylline altered the expression of c-fos and c-jun. While PDGF was found to induce the expression of both c-fos and c-jun, pentoxifylline was found to effectively reduce the effect of PDGF-induced c-jun gene expression, without altering c-fos gene expression. These results suggest that pentoxifylline inhibits PDGF-stimulated proliferation by decreasing c-jun expression. These results further suggest a variety of diseases and/or conditions which may also be successfully treated with compds., such as pentoxifylline, which reduce the transcription of c-jun gene.

L2 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:628573 HCAPLUS
DOCUMENT NUMBER: 129:340023
TITLE: Ultrastructural immunolocalization of basic fibroblast growth factor in mast cell secretory granules: morphological evidence for bFGF release through degranulation
AUTHOR(S): Qu, Zhenhong; Kayton, Robert J.; Ahmadi, Proochista; Liebler, Janice M.; Powers, Michael R.; Planck, Stephen R.; Rosenbaum, James T.
CORPORATE SOURCE: Casey Eye Institute, Oregon Health Sciences University, Portland, OR, USA
SOURCE: Journal of Histochemistry and Cytochemistry (1998), 46(10), 1119-1128
CODEN: JHCYAS; ISSN: 0022-1554
PUBLISHER: Histochemical Society, Inc.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors previously reported that mast cells (MCs) serve as a source of basic fibroblast growth factor (bFGF), a potent angiogenic and mitogenic polypeptide, suggesting that bFGF may mediate MC-related neovascularization and fibroproliferation. Unlike many other growth factors, bFGF lacks a classic peptide sequence for its secretion, and the mechanism(s) for its release remains controversial. Because MCs release a wide spectrum of bioactive products via degranulation, the authors hypothesized that MC degranulation may be a mechanism of bFGF release and used ultrastructural immunohistochem. to test the hypothesis. The authors reasoned that if bFGF is released through degranulation, it should be localized to MC secretory granules. Human tissues with chronic inflammation and rat/mouse tissues with anaphylaxis were studied. In all tissue samples examined, pos. staining (or immunogold particle localization) for bFGF in MCs was predominantly in the cytoplasmic granules. Moderate bFGF immunoreactivity was also found in the nucleus, whereas the cytosol and other subcellular organelles exhibited minimal immunogold particle localization. In contrast, no immunogold particle localization for bFGF was observed in lymphocytes or plasma cells. In rat/mouse lingual tissue undergoing anaphylaxis, immunogold particle localization for bFGF was found not only in swollen cytoplasmic granules but also in the extruded granules of MCs. Three different anti-bFGF antibodies gave similar immunogold particle localization patterns, whereas all controls were neg. These results provide morphol. evidence suggesting that, despite the lack of a classic secretory peptide in its structure, bFGF is localized to the secretory granules in MCs and may be released through degranulation.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:63735 HCAPLUS

DOCUMENT NUMBER: 128:149781

TITLE: Synthesis of basic fibroblast growth factor by murine mast cells

AUTHOR(S): Qu, Zhenhong; Huang, Xiaona; Ahmadi, Proochista; Stenberg, Paula; Liebler, Janice M.; Le, Anh-Chi; Planck, Stephen R.; Rosenbaum, James T.

CORPORATE SOURCE: Departments of Ophthalmology, Oregon Health Sciences University, Casey Eye Institute, Portland, OR, USA

SOURCE: International Archives of Allergy and Immunology (1998), 115(1), 47-54
CODEN: IAAIEG; ISSN: 1018-2438

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mast cells (MC) are involved in a wide spectrum of disorders characterized by neovascularization and fibroproliferation. The authors and others recently reported that human MC are a source of basic fibroblast growth factor (b FGF-2), a potent angiogenic and mitogenic polypeptide, in several disease conditions, such as chronic inflammation, hemangioma, and benign cutaneous mastocytosis. These finds suggest that FGF-2 may be an important mediator of cell proliferation and angiogenesis associated with MC. Since MC are heterogeneous across species, it is unknown whether FGF-2 expression is a feature common to all MC, or whether FGF-2 expression by MC can be regulated. The authors therefore examined FGF-2 expression by MC in mouse tissue and MC lines. Immunostaining, RT-PCR, ELISA, immunoblot and Northern blot analyses were employed to study four murine MC lines for FGF-2 expression and its regulation by transforming growth factor-β (TGF-β), stem cell factor (SCF), and tumor necrosis factor-α (TNF-α). Mouse tissue MC and three of four murine MC lines (CFTL-12, CFTL-15, ABFTL-3) express FGF-2 as judged by immunostaining, ELISA, Western blot and Northern blot analyses, and

reverse transcription-polymerase chain reaction. While TNF-α appeared to down-regulate FGF-2 mRNA levels, treatment with SCF or TGF-β resulted in an increase in the expression of FGF-2 at mRNA level which can be attenuated by TNF-α. However, the concurrent increase in FGF-2 protein was negligible, possibly due to immaturity of these cell lines. Expression of FGF-2 may be a ubiquitous feature of MC in other species in addition to humans, and can be selectively regulated by SCF, TGF-β and TNF-α.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:34155 HCAPLUS
DOCUMENT NUMBER: 128:139460
TITLE: The immunobiology of interferon-gamma inducible protein 10 kD (IP-10): a novel, pleiotropic member of the C-X-C chemokine superfamily
AUTHOR(S): Neville, Lewis F.; Mathiak, Guenther; Bagasra, Omar
CORPORATE SOURCE: XTL Biopharmaceuticals, Rehovot, 76100, Israel
SOURCE: Cytokine & Growth Factor Reviews (1997), 8(3), 207-219
CODEN: CGFRFB; ISSN: 1359-6101
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 100 refs. Interferon-γ inducible protein 10 kDa (IP-10) is a highly inducible, primary response gene that belongs to the C-X-C chemokine superfamily. Despite the original cloning of IP-10 in 1985, its biol. functions are still unclear although accumulating reports indicate that it is a pleiotropic mol. capable of eliciting potent biol. effects, including stimulation of monocytes, natural killer and T-cell migration, regulation of T-cell and bone marrow progenitor maturation, modulation of adhesion mol. expression as well as inhibition of angiogenesis. More interest is now likely to be focused on IP-10 due to the recent cloning of an IP-10 receptor. This paper aims to highlight the authors' current knowledge of IP-10 and its homologs as well as defining its likely involvement in regulating fibroproliferation following inflammatory lung injury.

REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:196745 HCAPLUS
DOCUMENT NUMBER: 126:258697
TITLE: Cyclosporine reduces development of obliterative bronchiolitis in a murine heterotopic airway model
AUTHOR(S): King, Melissa B.; Jessurun, Jose; Savik, S. Kay; Murray, Joel J.; Hertz, Marshall I.
CORPORATE SOURCE: Dept. of Internal Med., Univ. of Minnesota Medical School, Minneapolis, MN, 55455, USA
SOURCE: Transplantation (1997), 63(4), 528-532
CODEN: TRPLAU; ISSN: 0041-1337
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Obliterative bronchiolitis (OB), an important threat to the long-term survival of lung transplant recipients, is characterized histol. by fibroproliferation within small airways. The pathogenesis of OB is thought to involve chronic allograft rejection, and therapy frequently includes augmentation of immunosuppression. We have developed a model that reproduces the pathol. lesion of OB and allow study of interventions designed to limit airway fibrosis. In this model, heterotopic transplantation of murine airways into immune-mismatched recipients

results in epithelial abnormalities and fibroproliferation in the airway lumen, changes not seen in heterotopic isografts. Cyclosporine (CsA) inhibits activation and proliferation of T lymphocytes and is commonly administered after lung transplantation. We hypothesized that use of CsA in our model system would reduce fibroproliferation in tracheal allografts. To test this hypothesis, murine tracheas were transplanted heterotopically into allo-matched and allomismatched recipients, and then treated with varying doses (5, 10, 15, or 25 mg/kg i.p. q.d.) of CsA. Controls included allografts and isografts not treated with CsA. After 30 days, tracheas were harvested and examined histol. CsA markedly reduced the development of fibroproliferation in allografts (19% in treated allografts vs. 90% in untreated allografts, $P<0.0001$), but did not reduce inflammation or airway epithelial cell injury. High-dose (25 mg/kg/day) CsA was more effective than lower doses in reducing fibroproliferation (0% in high dose vs. 29% in low dose, $P=0.04$). These findings demonstrate that CsA significantly reduces development of the pathol. lesion of OB, and supports the role of alloimmunity in the pathogenesis of this disease.

L2 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:98756 HCAPLUS
DOCUMENT NUMBER: 126:127128
TITLE: The role of the host defense response in the progression and outcome of ARDS: pathophysiological correlations and response to glucocorticoid treatment
AUTHOR(S): Meduri, G. U.
CORPORATE SOURCE: Department of Medicine, Division of Pulmonary and Critical Care Medicine, The University of Tennessee, Memphis, TN, 38163, USA
SOURCE: European Respiratory Journal (1996), 9(12), 2650-2670
CODEN: ERJOEI; ISSN: 0903-1936
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The host defense response (HDR) to insults is similar regardless of the tissue involved and consists of an interactive network of simultaneously activated pathways that act in synergy to increase the host's chance of survival. Among this cascade of integrated pathways, three aspects of the HDR, inflammation, coagulation and tissue repair, are analyzed sep. to explain the histol. and physiol. changes occurring tat the tissue level in unresolving acute respiratory distress syndrome (ARDS). Cellular responses in HDR are regulated by a complex interaction among cytokines have concentration-dependent biol. effects. The degree of inital HDR may determine the progression of ARDS. On Day 1 of mech. ventilation and over time, nonsurvivors of ARDS have significantly higher plasma and bronchoalveolar lavage inflammatory cytokine levels than survivors. In the absence of inhibitory signals, the continued production by sustaining inflammation with tissue injury, intra- and extravascular coagulation and proliferation of mesenchymal cells (fibroproliferation) with deposition of extracellular matrix resulting in fibrosis. Glucocorticoids inhibit the HDR cascade at virtually all levels; their gradual and generalized suppressive influence protects the host from overshooting. In patients with exaggerated HDR, however, cytokine elevation may cause a concentration-dependent resistance to glucocorticoids by reducing glucocorticoid receptor binding affinity. Recent clin. and exptl. studies have shown that effective containment of the HDR in unresolving ARDS may be achieved only if glucocorticoid administration is prolonged. A double-blind randomized study is in progress to evaluate the role of prolonged glucocorticoid treatment in unresolving ARDS.
REFERENCE COUNT: 219 THERE ARE 219 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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L2 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:108472 HCAPLUS
DOCUMENT NUMBER: 124:172214
TITLE: Surfactant downregulates synthesis of DNA and inflammatory mediators in normal human lung fibroblasts
AUTHOR(S): Thomassen, Mary Jane; Antal, Joyce M.; Barna, Barbara P.; Divis, Lisa T.; Meeker, David P.; Wiedemann, Herbert P.
CORPORATE SOURCE: Dep. Pulmonary Crit Care Med. Immunol., Cleveland Clin. Found., Cleveland, OH, 44195-5038, USA
SOURCE: American Journal of Physiology (1996), 270(1, Pt. 1), L159-L163
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The initial inflammatory event in the adult respiratory distress syndrome (ARDS) is followed by fibroproliferation and a cascade of fibroblast-derived mediators. Because lung fibroblasts may be exposed to surfactant as well as inflammatory cytokines during ARDS, the authors hypothesized that surfactant might modulate fibroblast activity. The authors previously demonstrated that surfactant inhibited production of inflammatory cytokines from endotoxin-stimulated human alveolar macrophages. In the current study the effects of surfactant on normal human lung fibroblast proliferative capacity and mediator production were examined Both synthetic (Exosurf) and natural (Survanta) surfactant inhibited fibroblast [3H]thymidine incorporation. Examination of pre-S-phase events indicated stimulation of the immediate response gene, c-fos, and no effect on the G1/S cyclin, cyclin D1, suggesting that the surfactant block occurred elsewhere before S phase. The antioxidant N-acetyl-L-cysteine (NAC), like surfactant, inhibited [3H]thymidine incorporation. Furthermore, menadione, a generator of intracellular H2O2, stimulated fibroblast [3H]thymidine incorporation, and this was inhibited by surfactant. Interleukin-1 (IL-1)-stimulated secretion of the inflammatory mediators, IL-6 and prostaglandin E2, was also inhibited by surfactant. These data suggest that surfactant may modify lung fibroblast participation in ARDS sequelae by downregulating DNA synthesis and secondary inflammatory mediator production

L2 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:122085 HCAPLUS
DOCUMENT NUMBER: 118:122085
TITLE: Fibroblast growth factors in connective tissue disease associated interstitial lung disease
AUTHOR(S): Thornton, S. C.; Robbins, J. M.; Penny, R.; Breit, S. N.
CORPORATE SOURCE: Cent. Immunol., St. Vincent's Hosp., Australia
SOURCE: Clinical and Experimental Immunology (1992), 90(3), 447-52
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fibrosis is a major cause of morbidity and mortality in chronic inflammatory diseases, especially interstitial pulmonary disorders. Fibroproliferation is an important part of this fibrotic response, and is mediated largely through growth factors such as blood platelet-derived growth factor (PDGF), insulin-like growth factor (IGF) I, and tumor necrosis factor-α (TNF-α). Alveolar mononuclear cells were obtained from subjects by bronchoalveolar lavage and assessed for the spontaneous release of fibroblast growth factors. The humans had

different connective tissue disorders, both with and without inflammatory pulmonary complications. The lavage cells spontaneously secreted a fibroblast growth factor activity over 24 h, with the maximum activity detected at 6-12 h. The growth factor activity could be detected in most subjects with connective tissue disease-associated inflammatory lung diseases and some normal subjects, but the amount of growth factor activity was much higher in the former than in the latter group. Antibody depletion expts. showed that the growth factor activity from lavage cells of normal patients was attributable to TNF-α, while patients with interstitial lung disease secreted large amts. of PDGF and fibronectin in addition to TNF-α. Approx. 40-50% of the total released growth factor activity could be accounted for by PDGF, and 100% by the combination of PDGF, TNF-α, and fibronectin. While TNF-α was released from the bronchoalveolar lavage cells of many subjects, many patients with interstitial lung diseases also released spontaneously large amts. of fibroblast growth factor activity attributable to PDGF and fibronectin.

L2 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:509846 HCAPLUS
DOCUMENT NUMBER: 117:109846
TITLE: Role of Kupffer cells in developing streptococcal cell wall granulomas: streptococcal cell wall induction of inflammatory cytokines and mediators
AUTHOR(S): Manthey, Carl L.; Kossmann, Thomas; Allen, Janice B.; Corcoran, Marta L.; Brandes, Mary E.; Wahl, Sharon M.
CORPORATE SOURCE: Dep. Microbiol., Univ. Health Sci., Bethesda, MD, 20892, USA
SOURCE: American Journal of Pathology (1992), 140(5), 1205-14
CODEN: AJPAA4; ISSN: 0002-9440
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hepatic granulomas are induced by i.p. injection of streptococcal cell walls (SCW) into Lewis rats. Kupffer cells rapidly clear SCW from the blood, and the authors examined Kupffer cells further for a role in SCW-hepatic inflammation. Isolated Kupffer cells cultured with SCW secreted high levels of tumor necrosis factor α (TNFα), interleukin-1 (IL-1), transforming growth factor β (TGFβ), and prostaglandin E2 (PGE2). SCW transiently induced increased steady-state levels of IL-1β and TNFα mRNA; in contrast, constitutive expression of TGFβ1 mRNA in Kupffer cells was not affected by SCW. Low concns. of SCW induced the accumulation of intracellular IL-1 and TGFβ bioactivity, with intracellular IL-1 bioactivity remaining high through ≥72 h of culture. Kupffer cells isolated 1, 7, and 21 days after SCW injection did not express IL-1β or TNFα mRNA greater than control levels and exhibited marked hyporesponsiveness to secondary in vitro stimulation with SCW or lipopolysaccharide. SCW transiently induces Kupffer cells to secrete a variety of soluble mediators that contribute to hepatic inflammation by inducing leukocyte recruitment and activation and fibroproliferation. The transient nature of the Kupffer cell response and the hyporesponsiveness to secondary stimulation may be a mechanism by which the hepatic inflammation is neg. regulated.

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FILE 'HCAPLUS' ENTERED AT 11:57:36 ON 14 NOV 2006
L1 39 S FIBROPROLIFERATION AND INFLAMMAT?
L2 18 S L1 NOT PY>2001

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